

### **REMARKS**

The Office Action of March 20, 2009, has been carefully studied. Claims 10, 12-14 and 17 currently appear in this application. These claims define novel and unobvious subject matter under Sections 102 and 103 of 35 U.S.C., and therefore should be allowed. Applicant respectfully requests favorable reconsideration and formal allowance of the claims.

### **Claim Amendments**

Claim 10 has been amended by reciting a composition for use as a standard in detecting degradation products of ED-71, wherein the standard compound is the trans form of ED-71.

Claim 12 has been amended to recite "dl- $\alpha$ -tocopherol" rather than "an antioxidant." Support for this amendment can be found in the specification as filed at paragraph [0015].

### **Rejections under 35 U.S.C. 112**

Claims 12-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Examiner alleges that there is no description or guidance for suppressing the generation of isomers or for under shading.

This rejection is respectfully traversed.

Support for suppressing generation of degradation products, as claimed in amended claim 12, can be found in the specification as filed in paragraphs [0010] and [0011].

Specifically, these paragraphs describe the structure and the chemical name of the trans form (i.e., isomer) of ED-71 ((5E,7E)-(1R,2R,3R)-2-(3-hydroxypropoxy)-9,10-secocholesta-5,7,10(19)-triene-1,3,25-triol). Paragraph [0011] states as follows: "The generation of these degradation products can be suppressed in an oily preparation comprising ED-71 by adding an antioxidant thereto." Although the specification does not contain the term "method", one skilled in the relevant art would recognize this description as substantially describing the method of claim 12, since the step of adding an antioxidant is described therein. Regarding the term "dl- $\alpha$ -tocopherol", paragraph [0015] notes that this is the preferred antioxidant.

The term "generation of isomers" in claim 12 has been replaced with "the generation of a degradation product." This term appears frequently in the specification. For example, the following descriptions in the specification are noted:

In the present invention, "degradation product of ED-71" refers to main degradation products detected during the storage of ED-71 as an oily preparation.

In a state in which generation of the degradation product of ED-71 is suppressed, the amounts of each of the tachysterol and trans forms generated after 12-month storage at room temperature under shading is preferably 1% or less, more preferably 0.3% or less, and particularly preferably 0.1% or less.

These descriptions indicate that the “generation” of the degradation product means that the formation of a degradation product from ED-71 during the storage of ED-71 is suppressed during storage of ED-71. That is, in this context, “generation” is the same as “formation.”

As can be seen from the amended claims, the term “a degradation product” is limited to the trans form of ED-71 in claim 12. Generation or formation of the trans form is generically described, for example, in paragraph [0011] of the specification as filed, and is specifically described in Example 3 of the specification.

Specifically, Example 3 at paragraph [0063] describes that approximately 100 capsules were put into a vial and stored for 12 months under the conditions of 30°C/60% relative humidity and shading (i.e., protected from light). Table 3 at paragraph [0075] shows the formation of the trans form after storage under shading was suppressed to below the detection limit, N.D., by adding dl- $\alpha$ -tocopherol.

Therefore, the specification contains a specific example, teaching and guidance for suppressing the generation or formation of the trans form of ED-71 by adding dl- $\alpha$ -tocopherol.

Claim 13 finds support in the specification as filed at paragraph [0013]. The term "under shading" is described in paragraphs [0036], [0075], and the like. Although the meaning of the term is not specifically stated in the specification, it is clear to one skilled in the art that the term refers to placing the preparation in shade, that is, protected from light.

As an example of the method of claim 13, attention is directed to Example 4. Table 7 provided in Example 4 shows that even when dl- $\alpha$ -tocopherol was added in an amount of 0.002% by weight, the formation of the trans form of ED-71 was suppressed to below the detection limit, i.e., N.D., as compared with the control formulation. This is described in paragraph [0086] of Example 4, wherein the amount of the trans form generated was 0.1% or less in all regions in which the amount of dl- $\alpha$ -tocopherol added was 0.01% or more.

Accordingly, the descriptions in the specification are sufficient to convey to one skilled in the relevant art that the inventors had possession of the invention claimed in claims 12 and 13.

Claim 14 has been amended to recite “a standard of degradation product, which is also the trans form of ED-71.” The use of the isolated trans form of ED-71 as a standard of a degradation product, which is also the trans form of ED-71 formed during storage of ED-71, is described in paragraph [0065] of the specification as filed. This description shows a peak area ratio of trans form of ED-71 relative to the total sum of the detected peak areas, calculated and used as an index of the amount of the trans form formed during storage. In this description, the use of isolated trans ED-71 as a standard makes it possible to determine which one of a number of peaks of degradation products of ED-71 detected by HPLC analysis is that of the trans form of ED-71.

Accordingly, it is respectfully submitted that the descriptions in the specification are sufficient to convey to one skilled in the relevant art that the inventors had possession of the invention claimed in claim 14.

Claim 10 is drawn to a composition containing a standard for detecting degradation products of ED-71 in a sample. Claim 17 is drawn to a compound for synthesizing vitamin D compounds. The subject matter of claim 17 is described in paragraph [0019] of the specification as filed. Although the specification does not *in haec verba* describe synthesis of vitamin D compounds from this compound, because of the structural

closeness of the trans form of ED-71 to vitamin D derivatives one skilled in the relevant art can readily understand that the trans form of Ed-71 can be used to synthesize other vitamin D-based compound.

Accordingly, it is respectfully submitted that the descriptions in the specification are sufficient to convey to one skilled in the relevant art that the inventors had possession of the invention claimed in claim 10.

Claims 11-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is respectfully traversed.

Claim 11 has been cancelled.

As noted above, "generation" in claim 12 means "formation."

The Examiner is correct in that "shading" means that the preparation is covered, protected from exposure to light.

The "standard of isomer analysis" has been amended so "standard of a degradation product."

### **Art Rejections**

Claims 1 and 5-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al, WO 03/0047595, Miyamoto et al., US 4,666,643 and *Chem. Pharm Bull.* references.

This rejection is respectfully traversed.

Claim 10 has been amended to recite a composition for use as a standard in detecting degradation products of ED-71. This use is not disclosed in any of the cited references. Accordingly, claim 10 is patentable over the cited art.

Claims 12 and 13 are drawn to a method for suppressing generation of the trans form of ED-71 in an oily preparation comprising ED-71 by adding dl- $\alpha$ -tocopherol to the preparation. Submitted herewith is a declaration by Mr. Hisakazu Katsuki, that shows a dramatic effect on the suppression of formation of the trans form of ED-71 when dl- $\alpha$ -tocopherol is added to an oily preparation containing ED-71. It is clear from this declaration that dl- $\alpha$ -tocopherol is far more effective than other antioxidants, including BHA, catechin, ferulic acid, BTT, citric acid or thiolactic acid. This effect would not have been expected from the disclosures of the cited references, as these references do not differentiate

among the antioxidants in effectiveness in preventing formation of the  
trans form of ED-71.

In view of the above, it is respectfully submitted that the claims  
are now in condition for allowance, and favorable action thereon is  
earnestly solicited.

Respectfully submitted,

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